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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/602,272	02/16/1996	MICHAEL J. ELLIOTT	KIR96-01	4297

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/602,272	ELLIOTT ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *6,8-10,12-32 and 34-50* is/are pending in the application.

4a) Of the above claim(s) *16-28 and 38-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *6, 8-10, 12-15, 29-32, 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

2. Claims 6, 8-10, 12-32 and 34-50 are pending. Claims 16-28 and 38-50, drawn to non-elected inventions, remain withdrawn from consideration. Claims 6, 8-10, 12-15, 29-32, 34-37 are under consideration.

3. The rejection of claims 14, 15, 36 and 37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of applicants amendments. access number would overcome this rejection.

4. the rejection of claims 14, 15, 36 and 37 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

The specification lacks deposit information for the cA2 antibody on which the instant method claims depend. .One of skill in the art must know how to make and use the claimed monoclonal antibodies and it is not clear if the exact cell line producing the antibodies can be made without undue experimentation. Although the specification references US patents on page 8, lines 15-21 for the et al discloses how to use said monoclonals, this is not sufficient evidence that the monoclonal antibody cA2 of the instant specification will be publicly available during the enforceable life of a patent issuing from the instant application. Further, it is noted that none of the aforesaid patents (US 6,284,471, 5,656,272, 5,919,452, 5,698,195) have amended the respective specifications to reflect a Deposit number for the cA2 antibody. Thus, it appears that although said cA2 antibody has been disclosed by said patents, a deposit has not been made for patent purposes. Further, even if the aforesaid patents had made a deposit of the cA2 antibody,

this is insufficient to guarantee that the cA2 antibody would be publicly available during the enforceable life of a patent issuing from the instant application.

Exact replication of a cell line is an unpredictable event. Clark (Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man, 1993, page 1) states "The in vivo antibody response is heterogeneous and is made up of a large mixture of antibodies secreted from a polyclonal population of cells. In addition, because the differentiation of B cells involves the random rearrangements of gene segments and somatic mutation of these rearranged genes,....no two animals, even of an inbred strain will make an identical set of antibodies." It is unclear that one of skill in the art could derive antibodies identical to those claimed. Undue experimentation would be required to generate and screen all of the possible antibody and hybridoma species to obtained the claimed antibodies.

If deposits are made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney or record who has the authority and control over the conditions of deposit over his/her signature or registration number stating that the deposit has been accepted by an International Depository authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed from the depository as required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If deposits are not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If deposits are made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the deposited hybridomas are producing the monoclonal antibody cA2 as described in the specification as filed and are the same as those deposited in the depository, stating that the deposited hybridomas are producing the identical monoclonal antibody of cA2 as described in the specification and were in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re: Lundak, 773 F. 2d.1216, 227 USPQ 90 (CAFC 1985) and 37 CRF 1.801-1.809 for further information concerning deposit practice..

Applicant argues that the specification (page 8, lines 15-23) incorporates by reference information on cA2 to other US patent applications. This has been considered but not found persuasive. Information on cA2 described in other patent applications is no guarantee that the cA2 antibody will be publicly available for the life of the instant patent.

5. The rejection of claims 6, 8, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wakefield et al (Arteriosclerosis, Thrombosis and Vascular Biology, 1995, Vol. 15, pp. 258-268) in view of Arbustini et al (American Journal of Cardiology, 1991, Vol. 68,pp. B36-B50), as evidenced by the abstract of Riipi et al (Infection and Immunity, 1990, vol. 58, pp. 2750-2754) is maintained for reasons of record.

Claim 6 is drawn to a method of treating or preventing thrombosis in a subject diagnosed as suffering from thrombosis comprising administering a therapeutically effective amount of a tumor necrosis factor antagonist to the subject. Claim 29 is drawn to a method of decreasing

plasma fibrinogen in a subject diagnosed as suffering from thrombosis comprising administering a therapeutically effective amount of a tumor necrosis factor antagonist to the subject. Claims 8 and 30 encompass the antagonist as an anti-tumor necrosis factor antibody or an antigen-binding fragment thereof.

Wakefield et al teach a method wherein antibodies to TNF decreased the effect of ligation of the renal vein (page 259, first column, lines 2-4, under the heading "Animal Model and Protocol" and lines 1-7 in the second full paragraph under the above heading and page 262, under the headings of "Passive Immunization Studies (Group 2))). Wakefield et al teach that TNF was elevated as a result of the ligation in rats not receiving antibodies to TNF (page 261, second column, to page 262, first column, under the heading "Cytokine Expression Within the IVC During Thrombosis" and Table 2 on page 262). Wakefield et al do not teach the administration of the anti-TNF antibodies after a "diagnosis" thrombosis as Wakefield et al actively cause the thrombosis rather than deduce the presence of thrombosis as implied by the term "diagnosis".

Arbustini et al teach that thrombosis is common in patients having unstable angina and acute myocardial infarction (page 36B, second column , lines 5-9, under the abstract and page 40B, first column lines 1-3 under the heading "Incidence of thrombosis and plaque fissuring in acute versus chronic ischemic syndromes" and page 41B, Table VI). Arbustini et al hypothesize that vascular plaques undergo fissure which can be followed by thrombus formation, and identified alpha-TNF as an endogenous cytokine which is able to "damage" atherosclerotic plaques (page 37B, first column, lines 5-24). Arbustini et al agree with other reports in the literature which teach that the amount of TNF associated with a given lesion in a artery correlates with the severity of said lesion (page 48B, second column, lines 3-11). Arbustini et al teach that alpha-TNF was not found in normal coronary arteries.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer an anti-TNF antibody to a patient having unstable angina or undergoing acute myocardial infarction.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wakefield et al which indicate that an anti-TNF antibody can attenuate thrombus induction in an experimental rat model whereby thrombosis

was induced by mechanical means; and the teachings of Arbustini et al on the correlation between unstable angina and acute myocardial infarction and thrombosis, and on the further teachings of Arbustini et al which indicate the direct action of TNF to damage atherosclerotic plaques which would result in the fissuring of said plaque. Arbustini et al do not teach that all fissured plagues would necessarily produce a thrombus, however, one of skill in the art would be motivated to decrease the fissuring of any plaque in order to reduce or ablate thrombus formation, and thereby prevent arterial occlusion.

Further, the reduction of plasma fibrinogen in said subject diagnosed as suffering from thrombosis would be inherent in the method rendered obvious by the combination of Wakefield et al and Arbustini et al, as the method of decreasing plasma fibrinogen relies on the same method steps as the method of treating or preventing fibrosis. Further, the abstract of Riipi et al provides evidence that the anti-TNF antibody decreases plasma fibrinogen levels in vivo. Thus, the limitation of claim 29 and 30, drawn to a method of decreasing plasma fibrinogen are satisfied by the method rendered obvious by the combination of Wakefield et al and Arbustini et al.

6. The rejection of claims 6, 8-10, 12-15, 29-32, 34-37 under 35 U.S.C. 103(a) as being unpatentable over Wakefield et al (Arteriosclerosis, Thrombosis and Vascular Biology, 1995, Vol. 15, pp. 258-268) and Arbustini et al (American Journal of Cardiology, 1991, Vol. 68,pp. B36-B50) and the abstract of Riipi et al (Infection and Immunity, 1990, vol. 58, pp. 2750-2754) as applied to claims 6, 8, 29 and 30 above, and further in view of. Le et al (US 5,656,272, cited in a previous Office action) is maintained for reasons of record. The specific embodiments of the claims and the teachings of Wakefield et al and Arbustini et al and Riipi et al as applied to said claim limitations is set forth above.

Claims 10, 13, 32 and 35 specify the binding of the antibody to the epitopes consisting of amino acids 87-108 and 59-80 of human tumor necrosis factor. Claims 12 and 34 encompass a chimeric antibody comprising a non-human variable region specific for TNF and a human constant region. Claims 14 and 36 specify that the chimeric antibody inhibits the binding of TNF-alpha to the monoclonal antibody cA2. Claims 15 and 37 specify that the chimeric monoclonal antibody is cA2.

Le et al teach that the chimeric monoclonal antibody cA2 recognizes two peptide sequences of TNF-alpha consisting of the fragments defined by amino acids 87-108, and amino acids 87-108. Further, Le et al teach antibodies which compete with cA2 for binding to TNF-alpha (column 11, lines 39-50) and methods for obtaining said antibodies (column 17, lines 57-67), thus disclosing the embodiments of claims 14 and 36. Le et al teach that the administration of the chimeric version of the murine antibodies to humans overcomes the overcomes the problems of murine antibody immunogenicity and provides increased TNF neutralization activity (column 5, lines 19-22).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the cA2 antibody to a patient having unstable angina or undergoing acute myocardial infarction.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Le et al on the improvements of avoiding anti-murine anti-antibody response in human patients and the subsequence increase in antibody neutralization activity afforded by the administration of the cA2 antibody rather than a murine anti-TNF antibody.

7. Claims 6, 8, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wakefield et al (Arteriosclerosis, Thrombosis and Vascular Biology, 1995, Vol. 15, pp. 258-268) in view of Arbustini et al (American Journal of Cardiology, 1991, Vol. 68,pp. B36-B50) and Esser (WO 92/09203), as evidenced by the abstract of Riipi et al (Infection and Immunity, 1990, vol. 58, pp. 2750-2754) as applied to claims 6, 8, 29 and 30 above, and further in view of Esser (WO 92/09203).

The specific embodiments of the claims and the teachings of Wakefield et al and Arbustini et al and Riipi et al as applied to said claim limitations is set forth above. It is noted that claims 6 and 29 are broadly drawn to tumor necrosis factor antagonists and thus encompass methods comprising the administration of molecules which are broader in scope than anti-TNF antibodies.

Esser teaches the administration of inhibitors or TNF (for example, claim 1) for the treatment of diseases mediated by TNF (page 6, lines 1-7). Esser teaches that the disease state

can be a result of recessive or unregulated TNF production in a human (page 11, line 31 to page 12, line 4). Esser notes that TNF is a likely mediator of tissue injury in myocardial infarction and stroke. It is noted that Arbustini et al teaches that thrombosis is common in patients having acute myocardial infarction.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the inhibitors of TNF as taught by Esser to a patient having unstable angina or undergoing acute myocardial infarction.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wakefield and Arbustini et al who link elevated levels of TNF with thrombosis. Esser does not specifically teach that the TNF inhibitors are antagonists of TNF, however, the specification states on page 3, lines 2-5, that the TNF antagonists include compounds which prevent or inhibit TNF synthesis or release. Esser teaches that the THNF inhibitors inhibit the production of TNF by human monocytes, thus fulfilling the definition of TNF antagonist as set forth in the specification.

8. Applicant argues that the limitation of carrying out the claimed method in a subject "diagnosed as suffering from thrombosis" was not met by the combination of the prior art references. This has been considered but not found persuasive. It would be within the purview of one of skill in the art to apply a method of treating thrombosis to a subject in need thereof in order to decrease morbidity and mortality associated with thrombosis.

Applicant argues that the teachings of Wakefield et al are not pertinent to the instant invention because the animal model of Wakefield et al suggest that chronic venous insufficiency results in vein wall inflammation after the experimental induction of thrombosis. This has been considered but not found persuasive. Wakefield et al teach that chronic venous insufficiency is a result of the interrelation between thrombosis and inflammation. Wakefield et al teach that TNF alpha down regulates natural anti-coagulant mechanisms, such as protein C and S and the fibrinolytic system while inducing expression of pro-coagulant tissue factor on the surface of vascular endothelium supporting thrombosis [emphasis added] (page 258, second column, lines 2-13). Wakefield et al teach a method wherein antibodies to TNF decreased the effect of ligation of the renal vein. Thus the ligation of the renal vein produced a condition of thrombosis which

was ameliorated by anti-TNF antibodies. Wakefield et al states that anti-TNF antibodies were effective for attenuating the inflammatory events within the vein wall (page 258, second column, last sentence). Applicant argues that Wakefield et al does not teach or suggest methods of treating thrombosis (page 7, lines 21-22). This has been considered but not found persuasive. Wakefield et al teach that TNF supports thrombosis by down regulating anti-coagulant mechanisms which include the fibrinolytic system, and inducing expression of pro-coagulant factors on the surface of vascular endothelium. Wakefield concludes that TNF supports thrombosis and provides evidence that anti-TNF antibodies can neutralize the activity of TNF with respect to attenuating the inflammatory events within the vein wall. On of skill in the art would reasonably conclude that in patients suffering from thrombosis administration of anti-TNF antibodies would also attenuate the effects of TNF within the vein wall.

Applicant argues that the teachings of Arbustini do not overcome the deficiencies of Wakefield et al because Arbustini et al teaches that THF alpha was found in lipid rich plaques with or without thrombus. this has been considered but not found persuasive. Arbustini et al teach that "necrotizing cytokines able to damage plaque structure, such as tumor necrosis factor alpha have been detected in atherosclerotic plaques. "When spasm and vasoconstriction occur, such weak plaques could undergo shape modification, abnormal contact and rupture" Thus Arbustini et al teach that TNF association with plaques represents a potential for thrombus formation.

Applicant argues against the teaching of Riipi et al stating that Riipi et al do not mention the word thrombosis. This has been considered but not found persuasive. The abstract of Riipi et al clearly teaches that administration of TNF to mice results in an elevated fibrinogen level (abstract, lines 10-12). One of skill in the art would know that this teaching further substantiates the teaching of Wakefield et al on the downregulation of the anti-coagulant fibrinolytic system. One of skill in the art would conclude that downregulation of the fibrinolytic system results in an up regulation of fibrinogen which is substantiated by the abstract of Riipi et al.

Applicant argues that Le et al do not teach the treatment or prevention of thrombosis. Applicant is reminded that Le et al was not set forth in a 102 rejection of the instant claims. Because Le et al do not included thrombosis or "plasma fibrinogen" in their list of TNF alpha mediated pathologies and conditions, that somehow the teachings of Le et al cannot be applied

to the instant invention. This has been considered but not found persuasive. LE et al is relied upon only for the identity of the cA2 antibody which is disclosed by Le et al as binding TNF alpha.

Similarly applicant argues against the combination with Esser et al stating that Essner et al disclose only methods for treating TNF-mediated diseases with TNF inhibitors. this has been considered but not found persuasive. Essner et al is relied upon solely to demonstrate that the administration of TNF antagonists other than antibodies can effectively neutralize TNF.

9. The provisional rejection of claims 6, 8-10, 12-15, 29-32, 34-37 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 09/598,079 and claims 1-23 of copending Application No 09/754,004 and claims 32-54 of copending Application No. 09/921,937 and claims 1-20 of copending Application No. 10/252,489, all in view of Wakefield et al (Arteriosclerosis, Thrombosis and Vascular Biology, 1995, Vol. 15, pp. 258-268) and Arbustini et al (American Journal of Cardiology, 1991, Vol. 68,pp. B36-B50) as evidenced by the abstract of Riipi et al (Infection and Immunity, 1990, vol. 58, pp. 2750-2754). Claims 1-15 of the '079 application are drawn to methods of treating or preventing a tumor necrosis factor disease comprising the administration of a tumor necrosis factor antagonist, claims 1-23 of the '004 application are drawn to methods of treating a tumor necrosis factor mediated disease in an individual in need thereof comprising the administration of methotrexate and a tumor necrosis factor antagonist, claims 32-54 of the '937 application are drawn to a method for the treating or preventing a t tumor necrosis factor-mediated disease in an individual in need thereof comprising co-administration of methotrexate and a tumor necrosis factor antagonist to said individual in a therapeutically effective amount; claims 1-20 of the '489 application are drawn to a method of treating reoccurrence of a TNF-mediated disease in an individual having the TNF-mediated disease comprising the administration of multiple treatment cycles of anti-TNF antibody to said individual , wherein each treatment cycle is administered after loss of response to the previous cycle has occurred. All of these claims teach a method of treating TNF-mediated diseases. The claims to not teach thrombosis as a specific-TNF-mediated disease or the decrease of plasma fibrinogen levels by the administration of a TNF antagonist..

Wakefield et al teach thrombosis as a TNF-mediated disease because inhibition of the activity of TNF abrogates thrombosis in a rat experimental model.

Arbustini et al teach that TNF can damage plaques leading to fission and thrombosis and that TNF is not detected in normal arteries. Arbustini et al teach that thrombosis is characteristic of patients having unstable angina and acute myocardial infarction.

The abstract of Riipi et al teaches that the administration of anti-TNF antibodies decreases plasma fibrinogen levels, and thus is inherent in the administration of said antibodies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to carry out the methods of claims 1-15 of the '079 application or claims 1-23 of the '004 application or claims 32-54 of the '937 application or claims 1-20 of the '489 application to treat thrombosis in a patient having unstable angina or undergoing acute myocardial infarction.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Wakefield and Arbustini et al who link elevated levels of TNF with thrombosis and link thrombosis with acute myocardial infarction and unstable angina. Further, it would be inherent in the methods of claims 1-23 of the '004 application or claims 32-54 of the '937 application or claims 1-20 of the '489 application that the level of plasma fibrinogen would be decreased in said patients, as this is an inherent property of the claimed method which is evidenced by the abstract of Riipi et al that teaches an decrease in plasma fibrinogen levels after administration of an anti-TNF antibody.

10. Applicant argues that because the supporting references used in the double-patenting rejection were defected for the reasons argued against the 203 rejection, that the provisional double-patenting rejection was not properly set forth. This has been considered but not found persuasive for the reasons set forth above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
Art Unit 1642
03/22/04

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER